REMARKS

Claims 1, 12-17, 19-36, 38-46, 48-53, and 75-78 are pending in the present application.

At the outset, Applicants wish to thank Examiner Brooks and Examiner Richter for the helpful and courteous discussion with their undersigned Representative on July 7, 2009. During this discussion, various arguments (including those presented herein) were discussed. The content of this discussion is believed to be accurately reflected by the amendments and comments presented herein. Reconsideration of the outstanding rejections is requested in view of the amendments and remarks herein.

The rejection of Claims 1, 12-17, 19-36, 38-46, 48-53, and 75-78 under 35 U.S.C. §103(a) over Uchiyama et al (US 2002/0119164) in view of Kropf et al (US 6,858,214) is respectfully traversed.

In the Office Action, the Examiner now alleges that the claimed invention is obvious in view of the combined disclosures of Uchiyama et al in view of Kropf et al. The Examiner contends that Uchiyama et al disclose aqueous extracts of mushrooms, as well as particulates of these extracts. The Examiner further alleges that Uchiyama et al disclose that beta glucans are found in the extracts and that Kropf et al disclose that formulations containing beta glucans and have a particle size of 10 to 300 nm.

Applicants submit that Uchiyama et al is overly generic and insufficient to stand for the specific premise that the Examiner asserts. Specifically, Applicants submit that the claimed invention specifically relates to superfine particles of a β-glucan that is obtained from a water extract of a mushroom. In contrast, Uchiyama et al does not actually disclose or

suggest that the water extract disclosed therein contains any β-glucans. In fact, the paragraph [0034] disclosure by Uchiyama et al only relates to methanol extracts and specifically states that the β-glucans are only obtained in specific fractions obtained from this extract. There is nothing in Uchiyama et al to show that when *Agaricus blazei* are processed in accordance with the extraction method disclosed in paragraphs [0032] - [0033] that the fraction would contain any β-glucans or that the specific fractions containing β-glucans could or would be used for any specific purpose.

The Examiner is reminded that "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). Indeed, "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) In this case, there is no basis and/or evidence to provide a basis in fact and/or technical reasoning to reasonably support a determination that the extract disclosed in Uchiyama et al *necessarily* contains β-glucans, especially in view of the specific disclosure in paragraph [0034] that the β-glucans are only obtained in specific fractions obtained from this extract.

Even if the artisan would envision such a fraction and/or β-glucans would inherently be present in an aqueous extract of *Agaricus blazei* processed in accordance with the extraction method disclosed in paragraphs [0032] - [0033] of Uchiyama et al, this would only satisfy the first aspect of the claim. It must also be kept in mind that this specific extract would have to be formed into particles and those particles would have to be "superfine" (e.g.,

have an average particle diameter of 10 μm or less). Uchiyama et al is again overly general with respect to the meaning of particulates and, as such, fail to direct the artisan to particles as presently claimed.

Even if the disclosure at the end of paragraph [0033] of Uchiyama et al is viewed, which disclose that the products (i.e., the aqueous extract) can be "freeze dried or concentrated using water or methanol or acetone solutions" and as such could be interpreted as producing "particles" no reference is made to particle sizes and/or the importance of superfine particles. On page 5 of the Office Action, the Examiner recognizes this deficiency in the disclosure of Uchiyama et al in that this reference fails to disclose the particle size.

With respect to the particle size, Applicants submit that the citation of Kropf et al is misplaced for the reasons set forth in the response filed on January 29, 2009. Specifically, as previously argued, Kropf et al relates to yeast extracts not mushroom extracts which makes a substantial difference with respect to the nature and identity of the β-glucans.

Indeed, the claimed invention relates to a composition comprising superfine particles of a water extract of a mushroom, wherein the superfine particles have an average particle diameter of 10 μm or less, as determined in the form of a dispersion in water (Claim 1), a method of producing superfine particles comprising superfine pulverizing a β-glucan derived from a water extract of a mushroom (Claim 36), and a process for producing a composition containing superfine particles comprising superfine pulverizing a β-glucan derived from a water extract of a mushroom (Claim 42). Applicants submit that the only β-glucans disclosed or suggested by Kropf et al are yeast derived glucans. As recognized by the Examiner on page 4, lines 5-6 of the Office Action mailed March 25, 2008, Applicants submit that Kropf et al do not disclose or suggest water extracts of mushroom or β-glucans derived from a mushroom. Therefore, Kropf et al cannot affect the patentability of the claimed invention.

Despite the foregoing, the Examiner alleges on page 5, lines 17-20 of the Office Action mailed May 26, 2009, "one of ordinary skill in the art would have been motivated to formulate the *Agaricus blazei* extract (i.e., beta glucans) with the instant particle size (i.e., 10 μm or less) because it is well known in the art to formulate beta glucans with the instant particle size for cosmetic or dermatological purposes, as suggested by Kropf et al." Thus, it appears that the Examiner's position is that Kropf et al stands for the general premise that in similar art the artisan would recognize the desirability and general ability to prepare particles of β-glucans, including those disclosed by Uchiyama et al, having an average particle size within the claimed range. Applicants disagree for the reasons set forth in the response filed on January 29, 2009.

Much as in the preceding Office Actions, the Examiner's allegations completely fail to attempt and/or provide any evidence to establish that the β-glucans disclosed by Kropf et al, which are yeast derived glucans, are the same as those present in a water extract of mushrooms. Although not stated, it appears that it is the Examiner's position that the β-glucans disclosed by Kropf et al and obtained from yeast are inherently the same as the β-glucans derived from a water extract of a mushroom as in the claimed invention.

The Examiner is again reminded that "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). Indeed, "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) In this case, the Examiner has clearly

failed to meet this burden as the Examiner does not even attempt to offer any evidence to provide a basis in fact and/or technical reasoning to reasonably support a determination that the allegedly inherent characteristic necessarily flows from the teachings of Kropf et al.

The Examiner is further reminded that the shifting burden requires that the Examiner meet both parts of a two-part test: "Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, ***and*** the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference." (MPEP §2112(V)) This burden has not been met in this case as no evidence has been provided to show inherency.

Nonetheless, in the interest of expedient examination, Applicants submit that β-1,3-glucans derived from mushroom, in general, comprises β-1,6-glucans. On the other hand, β-1,3-glucans derived from yeast, does not comprise β-1,6-glucans. Thus, the β-glucans derived from mushroom is distinct from β-glucans derived from yeast as to the presence of β-1,6-glucans.

Support for the foregoing is provided by the following references, which were submitted on June 25, 2008:

1. Documents regarding Lentinula edodes (Shiitake) (Lentinan)

   Sasaki T., Takasuka N., Carbohydr. Res., 47, 99 (1976)

   Sasaki T., Takasuka N., Chihara G., Maeda Y. Y., Gann, 67, 191 (1976)

   Saito H., Ohki T., Sasaki T., Biochem. 16, 908 (1977)

2. Document regarding Schizophyllum commune (Sizofiran)

   Tabata K., Ito W., Kojima T. et al Carbohydr. Res., 89, 121 (1981)

3. Document regarding Selerotium (Seleroglucan)

   Falch B H, Espevik T, Ryan Let al. Carbohydr. Res., 329, 587 (2000)

In addition to the foregoing evidence that establishes that mushrooms comprise β-1,6-glucans the following references were filed with the response on January 29, 2009 to show that yeast disclosed by Kropf et al are devoid of β-1,6-glucans in addition to aforementioned references that show that the only β-glucans derived from yeast are β-1,3-glucans or β-glucans having both 1→3-linked and 1→6-linked glucose residues, which are distinct from the β-1,6-glucans derived from mushrooms:

a. "Zymosan", Wikipedia entry retrieved January 26, 2009 at http://en.wikipedia.org/wiki/Zymosan;

b. "β-glucan", Wikipedia entry retrieved January 27, 2009 at http://en.wikipedia.org/wiki/Beta-glucan;

c. Tada R, et al., Glycoconj. J. 25:851-861, 2008;

d. Oshiman K, et al., Planta Med. 8:610-614, 2002.

References (a) - (c) show that β-glucans derived from yeast are mostly β-glucans having β-1,3-linked main chains (partly, having β-1,6-linked branched chains (residues)). Reference (d) shows that β-glucans derived from mushroom has β-1,6-linked main chains, not β-1,6-linked as a residue.

Accordingly, Applicants submit that the extract disclosed by Kropf et al is inconsistent with and not compatible with the disclosure of Uchiyama et al. Accordingly, Kropf et al does not compensate for the deficiencies in the disclosure of Uchiyama et al.

Applicants submit that even if the combined disclosures of Uchiyama et al and Kropf et al did support a prima facie case of obviousness, which they do not, where a *prima facie* case of obviousness is found, Examiners must still "evaluate any evidence of secondary considerations". Indeed, MPEP 2145 directs Examiners as follows:

> If a *prima facie* case of obviousness is established, the burden shifts to the applicant to come forward with arguments and/or evidence to rebut the *prima facie* case. See, e.g., In re *Dillon,* 919 F.2d 688, 692, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990). Rebuttal evidence and arguments can be presented... **by counsel**, *In re Chu*, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995), **or by way of an affidavit or declaration under 37 CFR 1.132**, e.g., *Soni*, 54 F.3d at 750, 34 USPQ2d at 1687; *In re Piasecki*, 745 F.2d 1468, 1474, 223 USPQ 785, 789-90 (Fed. Cir. 1984). However, arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).
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> Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *Dillon*, 919 F.2d at 692-93, 16 USPQ2d at 1901... It may also include evidence of the state of the art, the level of skill in the art, and the beliefs of those skilled in the art. See, e.g., *In re Oelrich,* 579 F.2d 86, 91-92, 198 USPQ 210, 214 (CCPA 1978) (Expert opinions regarding the level of skill in the art were probative of the Nonobviousness of the claimed invention.);

It should also be noted that "Evidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness." No set number of examples of superiority is required. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987)"

To this end, Applicants **submit herewith** a Declaration under 37 C.F.R. §1.132 executed by Yasuyo Suga ("the Suga Declaration"). In the Suga Declaration, Applicants show that when the β-glucan derived from the water extract of a mushroom, which forms aggregates in an aqueous solution, is converted into the superfine particles having an average particle diameter of 10 μm or less (especially, by mixing with a dispersant) (see present claim

14, and page 27, line 19 to page 28, line 21), the resulting product significantly improved incorporation through mucosa so that immune functions can be activated or regulated. Such a result is not obtained when looking at the untreated β-glucan sample. In consideration of the evidence provided in the Suga Declaration, the Declarant further states:

> Unexpected results:
>
> (1) The stabilized fine particle can be prepared from the aggregate by treating β-glucan with lecithin under high temperature and high pressure.
>
> (2) The exertion of an inhibitory effect on tumor growth is dependent on a particle diameter. The critical point is 10 μm, and such effect is produced in case of a particle diameter of 10 μm or less.
>
> (3) β-glucan converted into superfine particle is absorbed in small intestinal Peyer's patch, whereas β-glucan, which is not converted into superfine particle, is not absorbed in small intestinal Peyer's patch.
>
> (4) β-glucan converted into superfine particle is absorbed in small intestinal Peyer's patch to produce an inhibitory effect on tumor growth.
>
> Reasons why these results would be considered unexpected:
>
> (1) For improving absorbability of a substance having a high molecular weight and poor absorbability, such as β-glucan, a method for converting into low molecular weight substance is generally selected.
>
> It is a novel idea that absorbability is poor due to large particle diameter in solution, and thereby such effect is not produced.
>
> There are no reports of a method for enhancing absorbability through a step of converting into superfine particle (instead of a step of converting into low molecular weight substance) to produce such effect, so far.
>
> (2) There are no reports of β-glucan, wherein intestinal absorbability is enhanced to produce such effect, so far.

Thus, the Suga Declaration clearly illustrates the criticality of the claimed particle size and in so doing rebut even a *prima facie* case of obviousness.

In view of the foregoing, withdrawal of this ground of rejection is requested.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

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